REMARKS

Status of the Claims

Pending claims

Claims 1 to 23, 40 to 55, 61 to 63, 65, 67 to 85, and 88 to 102 are pending (claims 24 to 39, and 56 to 60, 64, 66, 86 and 87 were canceled, without prejudice).

Claims canceled, added and amended in the instant amendment

Claims 1 to 23, 41, 42, 61, 63, 67, 68, 73 to 78, 82 to 85, 88, 93, to 100 are amended, claims 103 to 109 are added and claims 69 to 72 are canceled, without prejudice. Thus, after entry of the instant amendment, claims 1 to 23, 40 to 55, 61 to 63, 65, 67, 68, 73 to 85, and 88 to 109 will be pending.

Outstanding Rejections

Claims 3 to 5, 67 to 84, 97 and 99 are rejected under 35 U.S.C. §112, second paragraph. Claims 1, 3 to 21, 23, 40, 41, 67 to 85 and 93 to 102, are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification. Claims 1, 3 to 21, 23, 40, 41, 67 to 85 and 93 to 102, are rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled by the specification. Claims 16 to 21, 67 to 79, 82 to 85 and 93 to 97 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Wong, et al., GenBank Accession No. S72930, or, Taylor, et al., GenBank Accession No. X00520. Claims 1, 3 to 15, 23, 40, 41, 67 to 84 and 98 to 102, are rejected under 35 U.S.C. §102(b) as allegedly anticipated by priority document USSN 08/602,359, filed February 16, 1996, now USPN 5,942,430, whose corresponding PCT/US97/02039, published as WO 97/30160, on August 21, 1997. Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. For example, support for claims directed to nucleic acids having a sequence identity to an exemplary sequence, wherein the sequence identity is determined by a BLASTN algorithm, can be found, inter alia, on page 12, second full paragraph, of the priority document USSN 08/602,359, published as WO 97/30160.

The Patent Office alleged that there is no support in the priority document USSN 08/602,359, filed February 16, 1996, now USPN 5,942,430 (whose corresponding PCT/US97/02039, published as WO 97/30160, on August 21, 1997) for the genus of nucleic acids having 50% sequence identity to the exemplary SEQ ID NO:26 and encoding an esterase protein, as in claim 1 (see page 12, of the instant office action).

Applicants respectfully aver that the priority document inherently supports claims directed to nucleic acids having 50%, 55%, 60%, 65% or more sequence identity to the exemplary SEQ ID NO:26, or the nucleic acid encoding SEQ ID NO:36. For example, the priority document USSN 08/602,359, states "In accordance with one aspect of the present invention, there are provided novel enzymes, as well as active fragments, analogs and derivatives thereof" (see page 2, second full paragraph of WO 97/30160). USSN 08/602,359, also states: "The present invention also relates to nucleotide changes which result in amino acid substitutions, additions, deletions, fusions and truncations in the polypeptide encoded by the reference polynucleotide. In a preferred aspect of the invention these polypeptides retain the same biological action as the polypeptide encoded by the reference polynucleotide" (see page 12, third full paragraph). USSN 08/602,359, further states: "Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, within the scope of the appended claims, the invention may be practiced otherwise than as particularly described" (see page 33, last paragraph).

Applicants respectfully aver that because the invention was not intended to be limited to any exemplary percent sequence identity or to any particular "preferred embodiment," the priority document inherently supports the pending claims, including claims directed to nucleic acids having at least 50% sequence identity to SEQ ID NO:26.

Applicants note that support for claims directed to nucleic acids having at least 70%, 80%, 90%, 95% or 97% sequence identity to an exemplary sequence, can be found, inter alia, on page 12, second full paragraph, and page 15, third paragraph, of the priority document USSN 08/602,359, published as WO 97/30160.

Objections to the claims

Claims 1 to 23, 40, 41, 67 to 85 and 93 to 102, are objected to for including non-elected subject matter. The instant amendment addresses this issue.

Issues under 35 U.S.C. §112, second paragraph

Claims 3 to 5, 67 to 84, 97 and 99 stand rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The terms "high stringency", "moderate stringency" and "low stringency"

The Patent Office alleged claims 3 to 5 and 67 to 84 are indefinite because of the terms "high stringency", "moderate stringency" and "low stringency". The instant amendment addresses this issue. The terms have been deleted and replaced by specific hybridization conditions.

The phrase "from about 10 to 50 nucleotides in length ... "

The Patent Office alleged claims 67 and 82 to 84 are indefinite because of the phrase "from about 10 to 50 nucleotides in length ... ". The instant amendment addresses this issue. Note new claims 104 and 105.

The phrase "% sequence identity to the nucleic acid"

The Patent Office alleged claims 69 to 78 are indefinite because of the phrase "percent sequence identity to the nucleic acid." The instant amendment addresses this issue.

The Patent Office further alleged claims 67 to 84, 97 and 99 are confusing. The instant amendment addresses these issues.

Regarding claim 99, Applicants respectfully submit that fosmid vectors were well known in the art at the time of the invention, see, e.g., Kim (1995) "Construction and utility of a human chromosome 22-specific Fosmid library," Genet. Anal. 12(2):81-84, abstract attached.

Issues under 35 U.S.C. §112, first paragraph

Written Description

Claims 1, 3 to 21, 23, 40, 41, 67 to 85 and 93 to 102, are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification in

such as way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In particular, the Patent Office alleged, inter alia, that the claimed genus of polynucleotides is not disclosed in the specification because it is a large variable genus with a variety of variants, fragments and functions. It is alleged, inter alia, that many structurally and functionally unrelated nucleic acids are encompassed by the scope of the claims, and that a single species of the claimed genus is insufficient to put one of skill in the art in possession of all of the attributes and features of all species in the claimed genus.

Applicants respectfully submit that the claimed invention is sufficiently described in the specification such that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing. Applicants respectfully aver that a single species of a genus can be sufficient to put one of skill on the art in possession of all species with a claimed genus.

Applicants respectfully submit that only structurally and functionally related nucleic acids are encompassed by the scope of the claims. The nucleic acids of the claimed invention are described by structure (the exemplary sequences), a physico-chemical property (percent sequence identity and/or hybridization conditions) and function (esterase activity). All nucleic acids of the claimed genus must encode an enzyme having a percent sequence identity to an exemplary esterase coding sequence, or, hybridize under specific conditions to an exemplary esterase coding sequence. Applicants respectfully submit that describing a genus of polynucleotides in terms of physico-chemical properties (e.g., sequence identity or hybridization conditions) and function (e.g., encoding polypeptides having esterase activity) satisfies the written description requirement of section 112, first paragraph.

The Patent Office also alleged that a single species of a genus is insufficient to put one of skill on the art in possession of all species within a claimed genus. However, Applicants respectfully aver that even a single species of the instant invention is sufficient to put one of skill on the art in possession of the claimed genus. There is no bright line rule that a single species of a genus is insufficient to put one of skill on the art in possession of all species with a claimed genus. Applicants respectfully refer to the USPTO guidelines concerning compliance with the

written description requirement of U.S.C. §112, first paragraph. In example 14 of the guidelines (a copy of which is attached as Exhibit A), a claim reciting variants claimed by sequence identity to a sequence is sought (specifically, "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B). In the example, the specification is described as providing SEQ ID NO:3 and a function for the protein. The specification contemplates, but does not exemplify variants of SEQ ID NO:3 that can have substitutions, deletions, insertions and additions. Procedures for making proteins with substitutions, deletions, insertions, and additions are routine in the art and an assay is described which will identify other proteins having the claimed catalytic activity. The analysis of example 14 states that procedures for making variants (which have 95% sequence identity) are conventional in the art. The Guidelines conclusion states that the disclosure meets the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention.

Analogously, the genus of nucleic acids of the claimed invention is described by structure (the exemplary nucleic acids or polypeptide sequences), a physico-chemical property (percent sequence identity or stringent hybridization conditions) and function (having an esterase activity). All nucleic acids of the genus used in the claimed methods must have a percent sequence identity to an exemplary sequence of the invention (or, hybridize under specific conditions to an exemplary sequence of the invention). The USPTO guidelines recognize that written description is met for a genus of polypeptides described by structure, a physico-chemical property (e.g., a % sequence identity, hybridization under specific conditions) and a defined function (e.g., esterase activity), the genus of claimed polypeptides also meet the written description requirements of section 112.

The genus of nucleic acids of the claimed invention also fully comply with the requirements for written description of a genus of nucleic acids as set forth in University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997). In Lilly, the Court stated that, "[a] description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs....*or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.*" (emphasis added) Lilly, 43USPQ2d at 1406.

As noted above, the instant claims clearly set forth specific structural and physical characteristics of the claimed esterase-encoding nucleic acids. The claimed genus of polypeptides all must have esterase activity and a specific physical characteristic, e.g., a % sequence identity to the exemplary nucleic acid, or, hybridization under specific conditions to an exemplary sequence of the invention. Therefore, the genus of nucleic acids used in the claimed methods is defined via shared physical and structural properties in terms that "convey with reasonable clarity to those skilled in the art that Applicant, as of filing date sought, was in possession of invention." (Vas-Cath Inc. V. Mahukar, 19 USPQ2d 1111, (Fed Cir. 1991)).

More recently, the Federal Circuit stated

Similarly, in this court's most recent pronouncement, it noted:

> More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)].

Moba, B.V. v. Diamond Automation, Inc., 2003 U.S. App. LEXIS 6285; Fed. Cir. 01-1063, -1083, April 1, 2003.

Analogously, the function of the esterases encoded by the nucleic acids of the invention is sufficiently correlated to a particular, known structure (the exemplary sequences) and a physical (physico-chemical) property (percent sequence identity or specific hybridization conditions). Accordingly, the sequences used in the claimed methods are defined via shared physical and structural properties in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

Applicants also respectfully refer to recently issued claims directed to genuses of polynucleotides based on sequence identity (and stringent hybridization) to an exemplary nucleic acid, see, e.g., recently issued claims directed to, e.g., 72.5% sequence identity, as in USPN 6,593,514; 75% sequence identity, as in USPN 6,586,215; 80% sequence identity, as in USPN 6,596,926; 85% sequence identity, as in USPN 6,590,141 and USPN 6,586,179; 86% sequence

identity, as in USPN 6,583,337; 90% sequence identity (and "stringent hybridization"), as in USPN 6,541,684 (see Exhibit B).

Accordingly, Applicants respectfully submit that the pending claims meet the written description requirement under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are fully enabled by and described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Enablement

Claims 1, 3 to 21, 23, 40, 41, 67 to 85 and 93 to 102, are rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention.

The Patent Office states that the specification is enabling for the polynucleotide of SEQ ID NO:26 which encodes the esterase of SEQ ID NO:36.

However, it is alleged that the specification does not provide reasonable enablement for the large number of polynucleotides encoding esterases and variants and fragments broadly encompasses by the claims. The Patent Office alleged that it is not routine experimentation to screen for multiple substitutions or multiple modifications as encompassed by the claims. It is alleged that it would have required some knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate with esterase activity to create variants of an exemplary nucleic acid and test them for the expression of polypeptides having an esterase activity.

Applicants respectfully maintain that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, a genus of esterases to practice the claimed invention. As declared by Dr. Jay Short (see attached Rule 132 declaration), the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art, e.g., screening enzymes, and nucleic acids encoding enzymes, for esterase activity, was very high. As declared by Dr. Short, using the teaching of the specification, one skilled in the art could have selected routine methods known in the art at the time of the invention to express variants of nucleic acids encoding the exemplary enzyme of the invention and screen them for expression of polypeptides having esterase activity. Dr. Short declares that one skilled in the art

could have used routine protocols known in the art at the time of the invention, including those described in the instant specification, to screen for nucleic acids encoding polypeptides having a percent sequence identity to SEQ ID NO:26, or active fragments thereof, for esterase activity. Dr. Short declares that was routine to screen for multiple substitutions or multiple modifications of an enzyme-encoding sequence and predictably achieve positive results. As declared by Dr. Short, while the numbers of samples needed to be screened may have been high, the screening procedures were routine and successful results (i.e., finding variant nucleic acids encoding esterases) predictable.

Furthermore, Dr. Short declares that it would not have required any knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate with esterase activity to create variants of the exemplary nucleic acid and test them for the expression of polypeptides or peptides having esterase activity. Accordingly, it would not have taken undue experimentation to make and use the claimed invention, including identification of a genus of nucleic acids encoding esterases.

Whether large numbers of compositions (e.g., enzymes, antibodies, nucleic acids, and the like) must be screened to determine if one is within the scope of the claimed invention is irrelevant to an enablement inquiry. Enablement is not precluded by the necessity to screen large numbers of compositions, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit. The Federal Circuit in In re Wands directed that the focus of the enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" was set forth by the Federal Circuit in, e.g. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). In Hybritech, Inc., a single deposited antibody producing cell line enabled a claim generic to all IgM antibodies directed to a specific antigen. The Federal Circuit noted that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited

to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody specie was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, practitioners of the biological sciences for the instant invention also recognize the need to screen numbers of negatives to find a sample that has the desired properties, e.g., esterase-encoding activity. Furthermore, as declared by Dr. Short, the screening procedures used to identify nucleic acids within the scope of the instant invention (e.g., identifying nucleic acids encoding esterases) were all well known in the art and at the time this application was filed. All were routine protocols for the skilled artisan. Thus, the skilled artisan using Applicants' written disclosure could practice the instant claimed invention without undue experimentation.

Accordingly, Applicants respectfully submit that the pending claims meet the written description and enablement requirements under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are fully enabled by and described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §102

Wong, et al. or, Taylor, et al.

Claims 16 to 21, 67 to 79, 82 to 85 and 93 to 97 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Wong, et al., GenBank Accession No. S72930, or, Taylor, et al., GenBank Accession No. X00520. It is alleged that Wong et al., teaches a nucleic acid sequence (residues 655 to 671 of Wong) comprising a region identical to bases 351 to 368 of SEQ ID NO:26. It is alleged that Taylor, et al., teaches a nucleic acid sequence (residues 304 to 320 of Taylor) comprising a region identical to bases 536 to 552 of SEQ ID NO:26.

The instant amendment addresses this issue. After entry of the instant amendment, the claims will be drawn to, inter alia, a nucleic acid comprising at least 30 consecutive bases of a sequence as set forth in SEQ ID NO:26 or at least 30 consecutive bases of

a sequence having at least 70% identity to SEQ ID NO:26 and encoding a polypeptide having an esterase activity.

The priority document USSN 08/602,359

Claims 1, 3 to 15, 23, 40, 41, 67 to 84 and 98 to 102, are rejected under 35 U.S.C. §102(b) as allegedly anticipated by priority document USSN 08/602,359, filed February 16, 1996, now USPN 5,942,430, whose corresponding PCT/US97/02039, published as WO 97/30160, on August 21, 1997.

However, Applicants respectfully submit that claims 1, 3 to 15, 23, 40, 41, 67 to 84 and 98 to 102 can claim priority back to the priority document USSN 08/602,359, filed February 16, 1996. Applicants respectfully aver that the priority document inherently supports claims directed to nucleic acids having 50%, 55%, 60%, 65% or more sequence identity to the exemplary SEQ ID NO:26, or the nucleic acid encoding SEQ ID NO:36. For example, the priority document USSN 08/602,359, states "In accordance with one aspect of the present invention, there are provided novel enzymes, as well as active fragments, analogs and derivatives thereof" (see page 2, second full paragraph of WO 97/30160). USSN 08/602,359, also states: "The present invention also relates to nucleotide changes which result in amino acid substitutions, additions, deletions, fusions and truncations in the polypeptide encoded by the reference polynucleotide. In a preferred aspect of the invention these polypeptides retain the same biological action as the polypeptide encoded by the reference polynucleotide" (see page 12, third full paragraph). USSN 08/602,359, further states: "Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, within the scope of the appended claims, the invention may be practiced otherwise than as particularly described" (see page 33, last paragraph).

The invention claimed does not have to be described *in ipsis verbis* in order to satisfy the description requirement of § 112. In re Lukach, 442 F.2d 967, 968, 169 USPQ 795, 797 (CCPA 1971); Union Oil v. Atlantic Richfield, 208 F.3d 989, 54 U.S.P.Q. 2d 1227. If the specification contains a description of the claimed invention, albeit not *in ipsis verbis* (in the identical words), then the examiner or Board, in order to meet the burden of proof, must provide

reasons why one of ordinary skill in the art would not consider the description sufficient. In re Alton, 76 F.3d 1168, 37 U.S.P.Q.2D 1578 (Fed. Cir. 1996). See also MPEP §2163.

Applicants respectfully aver that because the invention was not intended to be limited to any exemplary percent sequence identity or to any particular "preferred embodiment," the priority document inherently supports the pending claims, including claims directed to nucleic acids having at least 50% sequence identity to SEQ ID NO:26. Thus, WO 97/30160, published August 21, 1997, is not prior art to these claims. Accordingly, this rejection under section 102(b) can be properly withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs, and 35 U.S.C. §102(b). Applicants respectfully submit that all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

In the event any necessary and additional fees fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050. Please credit any overpayment to this account.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 678-5070.

Respectfully submitted,

Date: Nov. 19, 2003

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